

- 52 -

CLAIMS

1. An isolated nucleic acid molecule comprising a nucleotide sequence having at least 65% identity to a degenerate variant of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 7.

5

2. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 7.

3. An isolated nucleic acid molecule comprising the complement of SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 7.

10

4. An isolated nucleic acid molecule encoding a ROR α 1-UNC5C polypeptide, said nucleic acid molecule comprising a nucleotide sequence having at least 65% identity to a degenerate variant of SEQ ID NO: 1 or SEQ ID NO: 3.

15

5. An isolated nucleic acid molecule encoding a ROR α 5 polypeptide, said nucleic acid molecule comprising a nucleotide sequence having at least 65% identity to a degenerate variant of SEQ ID NO: 7.

6. A vector comprising the nucleic acid molecule of any of claims 1-5.

20

7. A host cell comprising the vector of claim 6.

8. A purified fusion polypeptide of the ROR α 1-UNC5C polypeptide comprising an amino acid sequence having at least 65% identity to the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4.

25

9. The purified polypeptide of claim 8, wherein the amino acid sequence comprises the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4.

30

10. A purified polypeptide of the ROR α 5 polypeptide comprising an amino acid sequence having at least 65% identity to the amino acid sequence of SEQ ID NO: 8.

- 53 -

11. The purified polypeptide of claim 10, wherein the amino acid sequence comprises the amino acid sequence of SEQ ID NO: 8.

12. A method for producing a protein comprising:

- 5 a) culturing the host cell of claim 7 under conditions whereby the protein is produced,
 and
 b) recovering the protein from the host cell culture.

13. A method for detecting a polynucleotide which encodes a protein comprising the amino
10 acid sequence of SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO: 8 in a biological sample
comprising the steps of:

- a) hybridizing a complement of the polynucleotide sequence which encodes SEQ ID NO:
2, SEQ ID NO:4 or SEQ ID NO: 8 to a nucleic acid material of a biological sample, thereby
forming a hybridization complex; and
15 b) detecting the hybridization complex, wherein the presence of the complex correlates
with the presence of a polynucleotide encoding a protein in the biological sample.

14. A method for detecting the presence of an obesity susceptibility gene comprising:
 determining the identity of a gene located 20 cM, or less, adjacent to the
20 translocation breakpoint between chromosome 4 at cytoband 4q22.3 and chromosome 15 at
cytoband 15q22.2; and
 determining if the gene has aberrant gene expression as a consequence of the
translocation event.

25 15. A method for detecting the presence of a translocation junction between chromosome 4 at
cytoband 4q22.3 and chromosome 15 at cytoband 15q22.2 comprising analysing a sample of
DNA from an individual for the presence of the translocation junction.

16. A method for identifying a test compound that modulates the expression of an obesity
30 susceptibility gene identified in claim 14 comprising:
 contacting a cell capable of expressing the susceptibility gene with a test compound; and
 determining the level of expression of the obesity susceptibility gene in the presence of
the test compound, wherein a decrease or an increase in expression of a obesity susceptibility

- 54 -

gene, as compared to the level of expression of an obesity susceptibility gene in the absence of the compound, is indicative that the test compound modulates the expression of the obesity susceptibility gene.

5 17. A method of identifying a test compound that modulates the activity of an obesity protein encoded by the obesity susceptibility gene identified in claim 14, comprising:

contacting the obesity protein with a test compound; and

determining the level of activity of the obesity protein in the presence of the compound, wherein a decrease or an increase in obesity protein activity, as compared to the level of

10 activity of the obesity protein in the absence of the compound, is indicative that the test compound modulates obesity protein activity.

18. A method of treating a subject having obesity comprising administering an effective amount of the compound identified in claims 16 or 17.

15

19. Use of a compound identified in claims 16 or 17 in the preparation of a medicament for the treatment of obesity.

20. A pharmaceutical composition comprising a compound identified in claims 16 or 17, and
20 a pharmaceutically acceptable adjuvant, diluent or carrier.

21. A method of making a pharmaceutical composition comprising:

contacting a cell capable of expressing an obesity susceptibility gene with a test compound;

25 determining the level of expression of the obesity susceptibility gene in the presence of the test compound, wherein a decrease in expression of a obesity susceptibility gene, as compared to the level of expression of a obesity susceptibility gene in the absence of the compound, is indicative that the test compound decreases obesity susceptibility gene expression; and

30 formulating the test compound that decreases obesity susceptibility gene expression into a pharmaceutical composition.

- 55 -

22. A method of making a pharmaceutical composition comprising:
contacting an obesity protein with a test compound;
determining the level of activity of the obesity susceptibility protein in the presence of the compound, wherein a decrease in obesity protein activity, as compared to the level of activity
5 of the obesity protein in the absence of the compound, is indicative that the test compound decreases obesity protein activity; and
formulating the test compound that decreases obesity protein activity into a pharmaceutical composition.
- 10 23. A method for determining if an obesity susceptibility gene identified in claim 14 has an altered level of gene expression comprising:
comparing the level of obesity gene expression in a cell from a patient having obesity with a control cell, and
determining the level of expression of the obesity susceptibility gene in both cells,
15 wherein a decrease or an increase in expression of the obesity susceptibility gene, as compared to the level of expression of the obesity susceptibility gene in the control cell, indicates that the obesity susceptibility gene has altered gene expression.
24. A method of diagnosing obesity, or a susceptibility thereto in a subject, the method
20 comprising:
determining the level of mRNA of UNC5C; and
comparing the level of mRNA of UNC5C in the sample with a control, wherein an increase in the level of UNC5C in the sample compared to the control indicates that the subject has obesity , or a susceptibility thereto.
- 25
25. A method of diagnosing obesity or a susceptibility thereto in a subject, the method comprising:
determining the level of aUNC5C protein in a sample from a subject; and
comparing the level of UNC5C in the sample with a control, wherein an increase in the
30 level of the protein in the sample compared to the control indicates that the subject has obesity, or a susceptibility thereto.

- 56 -

26. A method of diagnosing obesity, or a susceptibility thereto in a subject, the method comprising analysing for the presence of ROR1 α 1-UNC5C mRNA, wherein the presence of the mRNA indicates that the subject has obesity, or a susceptibility thereto.

- 5 27. A method of diagnosing obesity or a susceptibility thereto in a subject, the method comprising analysing for the presence of the ROR1 α 1-UNC5C fusion polypeptide, wherein the presence of the polypeptide indicates that the subject has obesity, or a susceptibility thereto.